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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER
COLLINS, CYNTHIA E

ART UNIT	PAPER NUMBER
1638	

DATE MAILED: 03/29/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/025,145	STEELE ET AL.	
	Examiner	Art Unit	
	Cynthia Collins	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 January 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,7,8,67,75,82-88 and 91-97* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,67,75,82-88 and 91-97* is/are rejected.

7)☒ Claim(s) *7 and 8* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The Amendment filed January 10, 2005 has been entered.

Claims 2-6, 9-66, 68-74, 76-81 and 89-90 are cancelled.

Claims 1 and 67 are currently amended.

Claims 1, 7-8, 67, 75, 82-88 and 91-97 are pending and are examined.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

All previous objections and rejections not set forth below have been withdrawn.

Claim Rejections - 35 USC § 112

Claims 1, 67, 75, 82-88 and 91-97 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, for the reasons of record set forth in the office action mailed August 11, 2004.

Applicants' arguments filed January 10, 2005 have been fully considered but they are not persuasive.

Applicants note that claims 1 and 67 have been amended to recite that the (-)-camphene synthase encoded by the claimed nucleic acid molecules and vectors comprises an amino terminal half and a carboxy terminal half, wherein the carboxy terminal half comprises the amino acid sequence motif DDXXD, and that support for these claim amendments is found in the

specification at least at page 64, lines 31-32. Applicants submit that the claimed nucleic acid molecules are adequately described by: (1) the ability of the claimed nucleic acid molecules to hybridize under defined, stringent, hybridization conditions to a probe nucleic acid molecule, (2) the protein encoded by the nucleic acid molecule possesses (-)-camphene synthase; and (3) the presence of the characteristic sequence motif DDXXD within the carboxy terminal half of the encoded protein. Applicants note that an assay for identifying (-)-camphene synthase activity is described in the specification in Example 3. (reply page 5)

The recitation of a single encoded amino acid motif amino acid sequence motif comprising only five amino acids combined with the recitation that that the claimed nucleic acid molecules hybridize under defined, stringent, hybridization conditions to a probe nucleic acid molecule and possess (-)-camphene synthase activity does not overcome the rejection, because the specification does not describe a genus of sequences that encode a (-)-camphene synthase and that hybridize to the complement of the portion of SEQ ID NO:3 extending from nucleotide 1560 to nucleotide 1694 under hybridization conditions of 3 X SSC at 65°C for 16 hours followed by one wash in 0.5 X SSC at 55°C for 30 minutes, including an isolated nucleic acid molecule wherein the isolated nucleic acid molecule hybridizes to the complement of the portion of SEQ ID NO:3 extending from nucleotide 1560 to nucleotide 1694 under hybridization conditions of 5 X SSC at 65°C for 16 hours followed by two washes in 0.2 X SSC at 65°C for 20 minutes per wash, wherein the (-)-camphene synthase comprises a carboxy terminal half that comprises the amino acid sequence motif DDXXD.

Further, the description of an assay for identifying (-)-camphene synthase activity in the specification does not describe the claimed genus of sequences, since whether a sequence is

described is not dependent on whether the specification provides an enabling disclosure. See *University of California v. Eli Lilly*, 119 F.3d 1559, 43 USPQ 2d 1398 (Fed. Cir. 1997), which discusses the description of a claimed human cDNA sequence based on the disclosure of a rat cDNA sequence and a method for obtaining the human cDNA sequence:

> The patent describes a method of obtaining this cDNA by means of a constructive example, Example 6. This example, however, provides only a general method for obtaining the human cDNA (it incorporates by reference the method used to obtain the rat cDNA) along with the amino acid sequences of human insulin A and B chains. Whether or not it provides an enabling disclosure, it does not provide a written description of the cDNA encoding human insulin, which is necessary to provide a written description of the subject matter of claim 5. The name cDNA is not itself a written description of that DNA; it conveys no distinguishing information concerning its identity. While the example provides a process for obtaining human insulin-encoding cDNA, there is no further information in the patent pertaining to that cDNA's relevant structural or physical characteristics; in other words, it thus does not describe human insulin cDNA. Describing a method of preparing a cDNA or even describing the protein that the cDNA encodes, as the example does, does not necessarily describe the cDNA itself. (*Lilly*, 43 USPQ2d at 1405)

In the instant case, the description of an assay for identifying (-)-camphene synthase activity along with the description of the amino acid sequence of SEQ ID NO:65 does not provide a written description of the claimed genus of sequences.

Claims 1, 67, 75, 82-88 and 91-97 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated nucleic acid encoding the amino acid sequence of SEQ ID NO:65, a vector comprising said nucleic acid, a prokaryotic or plant or *Saccharomyces cerevisiae* host cell comprising said vector, and a method for enhancing the production of a (-)-camphene synthase of SEQ ID NO:65 in prokaryotic or plant or *Saccharomyces cerevisiae* host cell, does not reasonably provide enablement for other isolated nucleic acids encoding a (-)-camphene synthase, or for any unspecified eukaryotic host cell

comprising a vector comprising a nucleic acid encoding a (-)-camphene synthase , or for a method for enhancing the production of a (-)-camphene synthase in any unspecified eukaryotic host cell. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims, for the reasons of record set forth in the office action mailed August 11, 2004.

Applicants' arguments filed January 10, 2005 have been fully considered but they are not persuasive.

Applicants submit that one of ordinary skill in the art can readily identify plant species that produce (-)-camphene, and which therefore produce a (-)-camphene synthase that catalyzes the formation of the (-)-camphene. Applicants point, for example, to Attachment A, page 261 of the Merck Index (11th edition, 1989, Merck & Co., lnc., Rahway, New Jersey) that discloses that (-)-camphene occurs in many essential oils, such as in turpentine, in bergamot oil, in oil of citronella, neroli, ginger, and valerian. Applicants also point, for example, to Attachment B, The Essential Oils, Volume 11 (E. Guenther ed., R.E. Krieger, New York, N.Y., 1975) which discloses that "*d*-, *l*- and *dl*- camphene occur in nature quite widely distributed", and that *l*-camphene is found "in Siberian pine needle oil, in the oil distilled from the needles of *Abies concolor*, of *Pinus palustris*, in American and Russian turpentine oil, in Ceylon citronella oil, valerian oil, etc.". Applicants submit that the plants that produce (-)-camphene must, therefore, produce a (-)-camphene synthase that catalyzes the formation of the (-)-camphene. Consequently, Applicants submit that the prior art provides one of ordinary skill in the art with ample guidance to identify plant species from which to isolate a nucleic acid molecule encoding (-)-camphene synthase. (reply page 6)

Applicants' arguments that the prior art provides one of ordinary skill in the art with ample guidance to identify plant species from which to isolate a nucleic acid molecule encoding (-)-camphene synthase are unpersuasive. The claims are not directed to any nucleic acid molecule of any structure encoding encoding any (-)-camphene synthase of any structure. The claims directed to a genus of sequences that encode a (-)-camphene synthase having specific structural characteristics. The prior art cited by Applicants does not provide any guidance with respect to whether or not the (-)-camphene that is known to occur in certain plant species is produced by a (-)-camphene synthase that is encoded by a nucleic acid molecule that hybridizes to the complement of the portion of SEQ ID NO:3 extending from nucleotide 1560 to nucleotide 1694 under hybridization conditions of 3 X SSC at 65°C for 16 hours followed by one wash in 0.5 X SSC at 55°C for 30 minutes, including an isolated nucleic acid molecule wherein the isolated nucleic acid molecule hybridizes to the complement of the portion of SEQ ID NO:3 extending from nucleotide 1560 to nucleotide 1694 under hybridization conditions of 5 X SSC at 65°C for 16 hours followed by two washes in 0.2 X SSC at 65°C for 20 minutes per wash, wherein the (-)-camphene synthase comprises a carboxy terminal half that comprises the amino acid sequence motif DDXXD. Accordingly the prior art provides no guidance with respect to which plant species would be likely to possess the claimed (-)-camphene synthase coding sequences.

Applicants additionally submit that the present specification provides ample guidance for isolating a nucleic acid molecule encoding a (-)-camphene synthase from a plant source. Applicants point, for example, to Example 12, which describes probes and hybridization

conditions that can be used to screen nucleic acid libraries to identify nucleic acid molecules that encode monoterpene synthases, including (-)-camphene synthases. Applicants point, for example, to Example 3, which describes an assay that can be used to determine the principal product produced by a candidate monoterpene synthase protein that utilizes geranyl diphosphate as a substrate. Applicants point, for example, to pages 20-22, which disclose representative eukaryotic expression systems for expressing nucleic acid molecules that encode (-)-camphene synthase, to page 22, which describes representative methods for stably transforming a plant with a nucleic acid molecule that encodes a monoterpene synthase, such as (-)-camphene synthase, for expression of the protein therein, to page 26, which discloses representative methods for expressing monoterpene synthase proteins in prokaryotes. (reply pages 6-7)

Applicants' arguments that the disclosure of techniques such as nucleic acid hybridization, enzyme assays and transformation methods provides ample guidance for isolating a nucleic acid molecule encoding a (-)-camphene synthase from a plant source are unpersuasive. The outstanding rejection was not predicated on a failure to provide general guidance with respect to the application of techniques such as nucleic acid hybridization, enzyme assays and transformation methods. The outstanding rejection was predicated on a failure to provide specific guidance with respect to where and how to obtain the claimed isolated nucleic acid molecules that encode a (-)-camphene synthase having specific structural characteristics. As set forth at pages 7-8 of the prior office action, such guidance is necessary because one cannot predictably obtain the claimed nucleic acid molecules solely on the basis of the recited hybridization conditions. Absent guidance with respect to where and how to obtain the claimed isolated nucleic acid molecules, one skilled in the art would have to first identify and clone from

undisclosed sources nucleic acids that meet the structural limitations of the claims, and then test by trial and error the enzymatic activity of the protein encoded by each nucleic acid so obtained in order to discriminate between those nucleic acids that encode (-)-camphene synthases and those that do not. Such trial and error testing of sequences identified and cloned from undisclosed sources would constitute undue experimentation. The undue experimentation does not lie in the application of general techniques, such as nucleic acid hybridization, enzyme assays and transformation methods, but in the selection of particular sequences to be tested that both meet the specific structural limitations of the claims and are likely to have (-)-camphene synthase activity.

Applicants further submit that the prior art, and the teachings of the present specification, provide ample guidance for expressing a nucleic acid molecule encoding a (-)-camphene synthase in any eukaryotic cell. Applicants submit that undue experimentation is not required to identify eukaryotic cell types that tolerate expression of (-)-camphene, and in this regard point to Attachment C, the declaration of inventor Rodney B Croteau. Applicants submit that the Croteau Declaration describes the successful expression of a (-)-camphene synthase cDNA, and production of (-)-camphene, in eukaryotic *Saccharomyces cerevisiae* cells. (reply page 7)

The Examiner first notes that neither the declaration nor Applicants' reply indicate under what rule or statutory provision the declaration is submitted. Because the declaration provides evidence submitted to traverse the outstanding rejection, it is assumed that the declaration is submitted under 37 CFR § 1.132. Clarification by Applicants on this point is requested.

The Examiner acknowledges that the declaration of inventor Rodney B Croteau discloses the expression of a (-)-camphene synthase cDNA of SEQ ID NO:64, and the production of (-)-camphene, in the yeast *Saccharomyces cerevisiae*. The Examiner maintains, however, that the disclosure of the expression of a (-)-camphene synthase cDNA and the production of (-)-camphene in a single species of eukaryotic cell does not support the enablement of the full scope of the claims, which encompass methods of enhancing the production of (-)-camphene synthase in any unspecified type of eukaryotic cell. As set forth at pages 8-9 of the prior office action, the effect of expressing a nucleic acid encoding a (-)-camphene synthase in any unspecified eukaryotic cell is unpredictable, since monoterpenes such as camphene that would be produced as a consequence of (-)-camphene synthase expression are known to be toxic to certain types of eukaryotic cells. Absent guidance with respect to the type of eukaryotic host cell in which to express an isolated nucleic acid molecule encoding a (-)-camphene synthase, one skilled in the art would have to test by trial and error the effect of expressing such nucleic acids in the various different types of eukaryotic host cell systems available (mammalian, fungal, insect, etc.) in order to discriminate between those host cell systems in which (-)-camphene synthase production would be enhanced upon its expression and those that would not. Such trial and error testing of the effect of expressing nucleic acid molecules encoding (-)-camphene synthases in undisclosed host cell systems would constitute undue experimentation.

Allowable Subject Matter

Claims 7 and 8 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Remarks

Claims 7 and 8 are objected to.

Claims 1, 67, 75, 82-88 and 91-97 are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Cynthia Collins whose telephone number is (571) 272-0794. The examiner can normally be reached on Monday-Friday 8:45 AM -5:15 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on (571) 272-0804. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Cynthia Collins
Examiner
Art Unit 1638

CC

Cynthia Collins 3/25/05